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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,739	07/03/2003	Arthur M. Krieg	C01037.70043.US	4713

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/613,739	KRIEG, ARTHUR M.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/03/03, 10/31/03, 12/19/05, 3/09/06 and 7/03/06.*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,17-21,23,28,29,31,32 and 44, now 1-9, 16-20, 22, 17-28, 30-31 and 43.* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/29/04 and 10/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. It is noted that the previous examiner of record, Examiner Timothy M. Brown, has vacated the restriction requirement issued 11/15/2005. Hence, any response(s) filed to said restriction requirement is no longer of significance.

2. Applicant's election with traverse of Group I in the reply filed on 03/09/2006, in response to the restriction requirement filed 02/07/2006, is acknowledged. Applicant's election is: Group I, viral antigen, hepatitis B antigen, parenteral route, and alum adjuvant. Applicant also notes that Applicant's election embraces claims 1-8, 12-13, 17-21, 23, 28-29, 31-32 and 44. The traversal is on the ground(s) that a search and examination of the inventions listed as Groups I-III would not impose a serious burden on the examiner since the inventions embraces the same subject matter, an immunostimulatory nucleic acid comprising SEQ ID NO: 1.

Applicant's submission has been considered, however, it is not found persuasive. MPEP § 803 [R-3] provides the following: Under the statute, the claims of an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate pat-ents and they are either independent (MPEP § 802.01, § 806.06, and § 808.01) or distinct (MPEP § 806.05 - § 806.05(j)).

In the instant, while the inventions listed as Groups I-III are related as products which share an alleged common utility of antigen-specific immunomodulatory activities, but the common utility is not linked to a substantial structural feature. The products in this relationship are distinct if either or both of the following can be shown: (1) that the

products encompass embodiments that are not required to perform the common utility or (2) that the products as claimed can be used to perform another utility. In this case, the products as claimed can be used to perform another utility. For example, the product of Group I can be used to induce an immune response directed at a microbial agent; whereas, the product of Group II can be used to induce an immune response directed at a cancer, and the product of Group III can be used to induce an immune response directed at an allergen. Thus, the products as claimed can be used to perform a utility that is different from one another. Hence, the inventions listed as Groups I-III are distinct from the other.

Furthermore, because the inventions are distinct from one another, a different field of search would be required for each of the listed inventions. For example, the field of search for the invention of Group I includes the microbial agent; whereas, the field of search for the inventions of Group II-III include cancer antigen and allergen, respectively. In the instant, microbial agents, cancer agents and allergens do not overlap in scope; hence, a different field of search is necessary for each of the listed invention.

In summation, the inventions are distinct from one another for the reason(s) set forth above, and because of the differing field of search among the inventions, an examination of the inventions set forth in Groups I-III cannot be made without serious burden. The requirement is still deemed proper and is therefore made FINAL.

Applicant's request for the rejoinder of Group V, VI, VII and/or VIII should claim 1 be found allowable, provided that the claims of Group V, VI, VII and/or VIII depend from

or otherwise recite all the limitations of the allowable product claim is noted. In the instant, the Office has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the Office before the patent issues. See MPEP § 804.01.

Status of Claims

3. Claims 22, 24-27, 34-43, 45, 59-63, 67-70, 75-76, 82-83, 86-88, 91-94 and 97 are cancelled, per Applicant's 10/31/2003 submission. Claims 1-21, 23, 28-33, 44, 46-58, 64-66, 71-74, 77-81, 84-85, 89-90, 95-96 and 98-99 are pending. Claims 10-15, 30, 33, 46-58, 64-66, 71-74, 77-81, 84-85, 89-90, 95-96, and 98-99 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 03/09/2006. Claims 1-9, 17-21, 23, 28-29, 31-32 and 44 are under examination. [Note: To simplify the initial identification of the claims, the claims listed in this paragraph is as presented (numbered) by Applicant. For the correct numbering of the claims, see paragraph no. 5 of this office action.]

Specification

4. The disclosure is objected to because of the following informalities: The specification contains two contradictory descriptions of Figure 15A. Correction is required.

5. Additionally, the numbering of the claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). In the instant, claims 17-21, 23, 28-29, 31-32 and 44 have been

misnumbered by a single digit. The numerical value of these claims is off by a value of 1. In the instant, the Office notes that claim 16 is missing from the originally filed claim listing and the preliminary amendment filed 10/31/2003. Thus, claims 17-21, 23, 28-29, 31-32 and 44 have been renumbered 16-20, 22, 17-28, 30-31 and 43. Appropriate correction is required.

Information Disclosure Statement

6. The information disclosure statement filed 03/21/2005 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. In the instant, the Office cannot locate a copy of a PTO-1449 submitted with the 03/21/2005 IDS submission. The Office regrets any inconvenience this may cause Applicant, however, Applicant is hereby requested to provide a copy of the PTO-1449 submitted. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered.

7. Additionally, it is noted that a complete translation of the reference listed as item B2, on the IDS filed 04/29/2004 is not provided. Only an English version of the abstract is provided for said reference. Hence, in view of this, the consideration of the reference

listed as B2 on the IDS filed 04/29/2004 is limited to the content provided in the English translation of the abstract.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-9, 16-20, 22, 17-28, 30-31 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted element is: a limitation setting forth that the CpG motif present in the immunostimulatory nucleic acid molecule be unmethylated. In the instant, it is well understood that the immune stimulatory effects of immunostimulatory nucleic acid molecule are the result of the presence of unmethylated CpG dinucleotides. Hence, the presence of unmethylated CpG dinucleotides is essential for the immunostimulatory effects of immunostimulatory nucleic acid molecule. Thus, in the absence of language in the claims that expressly set forth that the immunostimulatory nucleic acid molecule comprises unmethylated CpG dinucleotides or a showing that unmethylated CpG dinucleotides are not necessary for this activity, the claims are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements.

Additionally, claim 7 recites the limitation "nucleic acid vector" in line 1 of the claim. There is insufficient antecedent basis for this limitation in the claim. In the instant, claim 7 recites a dependency to claim 3. Claim 3 does not reference any

nucleic acid vector. Hence, there is insufficient antecedent basis for the limitation set forth in the recitation "The composition of claim 3, wherein the nucleic acid vector". For the purpose of advancing examination of the instant patent application, claim 7 is interpreted to de a dependent of claim 6, which adequately provides proper antecedent basis for the recitation "nucleic acid vector".

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-9, 16-20, 22, 17-28, 30-31 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krieg et al.[1]

The claims are directed toward a composition comprising an immunostimulatory nucleic acid comprising the nucleic acid sequence of SEQ ID NO:1. Claim 3, which depends on independent claim 1, requires the composition to further comprise an antigen, which is later limited to a microbial antigen by claim 4. Claim 5 further limits the microbial antigen of claim 4 to a viral antigen. Claim 6 additionally limits the antigen of claim 3 to those encoded by a nucleic acid vector. Claim 7, which is interpreted to recite a dependency to claim 6, requires that the nucleic acid vector be different from the immunostimulatory nucleic acid. Claim 8 further limits the antigen of claim 3 to a peptide antigen. Claim 9, which depends on claim 1, requires the composition to further

comprise an adjuvant. Claim 16 (currently incorrectly listed as claim 17) requires the immunostimulatory nucleic acid to have a nucleic acid backbone that is modified. Claim 17 (currently incorrectly listed as claim 18), which depends on claim 16, requires the modification to be a phosphorothioate modification. Claim 18 currently incorrectly listed as claim 19), which depends on claim 16, requires the modified backbone to a chimeric backbone. Claim 19 (currently incorrectly listed as claim 20), which depends on claim 16, requires the immunostimulatory nucleic acid to have all modified backbones. Claim 20, (currently incorrectly listed as claim 21), which depends on claim 1, requires the composition to comprise a pharmaceutically acceptable carrier. Claim 22 (currently incorrectly listed as claim 23), which depends on claim 1, requires the immunostimulatory nucleic acid to comprise at least four CpG motifs. Claim 27 (currently incorrectly listed as claim 28), which depends on claim 1, requires the immunostimulatory nucleic acid to be formulated as a nutritional supplement. Claim 28 (currently incorrectly listed as claim 29), which depends on claim 28, requires the supplement be formulated as a capsule, pill, or a sublingual tablet. Claim 30 (currently incorrectly listed as claim 31), which depends on claim 1, requires the immunostimulatory nucleic acid be formulated for parenteral administration. Claim 31 (currently incorrectly listed as claim 32), which depends on claim 1, requires the immunostimulatory nucleic acid be formulated in a sustained released device. Claim 43 (currently incorrectly listed as claim 44), further limits the sustained release to a microparticle.

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[1] Krieg et al. WO 2001/22972, published April 05, 2001.

Additionally, claim 2, which depends on claim 1, limits the immunostimulatory nucleic acid sequence to consist of SEQ ID NO: 1. SEQ ID NO: 1 has the following sequence: TCGTCGTTTCGTCGTTTTGTCGTT.

Krieg et al. teaches a composition comprising of an immunostimulatory nucleic acid, wherein the immunostimulatory nucleic acid sequence consists of the sequence: TCGTCGTTTCGTCGTTTTGACGTT, SEQ ID NO: 888. SEQ ID NO: 888 of Krieg et al. has at least 4 CpG motifs and is 24 nucleic acid resides in length. The number of CpG motifs and nucleic acid residues present in SEQ ID NO: 888 of Krieg et al. is the same as that of Applicant's claimed SEQ ID NO: 1. The difference between SEQ ID NO: 888 of Krieg et al. and Applicant's claimed SEQ ID NO: 1 is: Nucleic acid residue at position 20 of the sequences are not the same. Nucleic acid residue at position 20 of SEQ ID NO: 888 of Krieg et al. is A (adenine), and the nucleic acid residue at position 20 of Applicant's claimed SEQ ID NO: 1 is T (thymidine). However, Krieg et al. suggests the exchange of the adenine with thymidine. [Lines 19-20, page 143, in particular.] Krieg et al. notes that the exchange resulted in slightly higher immunostimulatory activity induced by the immunostimulatory nucleic acid. Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to have exchanged adenine for thymidine. One of ordinary skill in the art at the time the invention was made would have been motivated to do so enhance the immunostimulatory activity of the immunostimulatory nucleic acid. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation

of success for doing so because Krieg et al have demonstrated the enhancement of immunostimulatory activity.

Krieg et al. further teaches the addition of an antigen to the composition. [Lines 19-21, page 6; Lines 3-5, page 38, in particular.] The antigen that Krieg et al. teaches includes microbial antigens, viral antigens, antigens encoded by a nucleic acid vector, and a peptide antigen. [Claims 38-39, page 160, in particular.] The nucleic acid vector that Krieg et al. teaches is different from the immunostimulatory nucleic acid. Krieg et al. also teaches the use of adjuvants with the composition. [Lines 15-16, page 94, in particular.] Krieg et al. additionally teaches the use of nucleic acid backbones that are modified. [Claim 18, page 158, in particular.] The modified backbone that Krieg et al. teaches includes phosphorothioate backbones and chimeric backbones. [Claims 19-20, page 158, in particular] Krieg et al. also teaches modifying all the backbones. [Claim 21, page 158, in particular.]

Krieg et al. also teaches the addition of a pharmaceutically acceptable carrier with the composition. [Lines 1-3, page 3, in particular.] Krieg et al. further teaches that the composition be formulated as a nutritional supplement. [Lines 25-28, page 6, in particular] Krieg et al. teaches that the supplement be formulated as a capsule, pill, or a sublingual tablet. Krieg et al. further teaches providing the composition in a form ready for parenteral administration. [Lines 10-15, page 13, in particular.] Krieg et al. additionally teaches the sustained release, specifically microparticle, form of the composition. [Lines 12-13, page 10, in particular.]

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Emily Le 9/12/06
Emily Le
Patent Examiner
Art Unit 1648

Continuation of Disposition of Claims: Claims pending in the application are 1-21,23,28-33,44,46-58,64-66,71-74,77-81,84,85,89,90,95,96,98 and 99, as presented by Applicant.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 10-15,30,33,46-58,64-66,71-74,77-81,84,85,89,90,95,96,98 and 99, as presented by Applicant.